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Review article

Rapid sequence intubation in high-risk patients: what clinicians and researchers must know – a narrative review

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ABSTRACT

Rapid sequence intubation (RSI) remains a cornerstone of airway management in critically ill patients, aiming to optimize oxygenation and ventilation, reduce the risk of secondary brain injury, and prevent gastric aspiration. Originally designed to minimize the interval between loss of airway reflexes and airway protection, while also limiting hemodynamic complications, RSI is now widely used in the operating room, intensive care unit, and emergency department. While aspiration prevention has historically been a central rationale for RSI, emerging evidence suggests that RSI may not significantly reduce this risk and may, in fact, be associated with increased rates of hypoxemia and hemodynamic instability. Pharmacological approaches, airway management techniques, and team-based preparation must be tailored to mitigate these complications. Contemporary RSI involves thorough preintubation assessment, preparation, and teamwork, emphasizing first-pass intubation success, patient positioning, apneic oxygenation, and gentle ventilation when appropriate. Several interventions have shown a clinically significant reduction of adverse events, such as the use of a video laryngoscope, apneic bag mask ventilation, or non-invasive ventilation for pre-oxygenation. The main recommended medications include a sedative (etomidate or ketamine are favored over propofol in hemodynamically unstable patients) and a paralytic (rocuronium or succinylcholine). Human factors, team-based preparation, and first-pass success remain key determinants of RSI outcomes. This narrative review synthesizes current evidence on RSI, highlighting pharmacological strategies, airway management techniques, and human factors, reflecting a shift from rigid protocols toward a more flexible, patient- and team-centered approach that balances aspiration risk with the prevention of desaturation and hypotension.
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Introduction

Rapid sequence intubation (RSI) is a widely adopted airway management technique primarily used in patients with acute respiratory distress requiring ventilatory support. It is also employed to reduce the risk of tracheal aspiration of gastric contents and to minimize the risk of secondary insult in brain injury [1]. RSI involves the administration of a hypnotic agent and a neuromuscular blocking agent [1]. Although RSI is traditionally performed in the controlled environment of the operating room (OR), its application has expanded to less controlled settings such as prehospital care, emergency departments (EDs), and intensive care units (ICUs). These environments are often characterized by resource constraints, hemodynamic instability, limited time for airway evaluation or preoxygenation, and complex comorbidities, all of which may pose unique challenges for RSI and potential contraindications to commonly used medications.

Recent advancements in RSI emphasize not only optimized pharmacologic strategies, such as appropriate drug selection and dosing, but also the integration of techniques, including videola-

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ryngoscopy (VL), stylets or bougies, noninvasive ventilation (NIV), and point-of-care ultrasound (POCUS) to reduce the risk of complications. This narrative review synthesizes current evidence surrounding pharmacologic agents and supportive interventions to enhance RSI safety and efficacy in high-risk patients and acute care settings. Recent developments in ventilation management have been outlined in a separate, recently published review [2].

Epidemiology and indications for RSI

Patients may present for elective procedures having observed an appropriate fasting interval, yet remain at elevated risk for aspiration due to underlying medical comorbidities. Certain conditions predispose these patients to impaired gastric emptying or increased risk of regurgitation and aspiration despite standard fasting precautions. These include the presence of a hiatal hernia, symptomatic gastroesophageal reflux disease (GERD), a history of bariatric surgery, or delayed gastric emptying as seen in poorly controlled diabetes mellitus [3]. For these conditions, it is usually recommended to proceed with RSI due to the high aspiration risk despite adequate fasting times. Of note, clear liquid emptying is generally preserved in patients with diabetic gastroparesis [4].

In the setting of emergent procedures performed in the OR, it is common for patients not to have been fasted for at least 6 h, which inherently increases the risk of aspiration. However, even when an appropriate fasting interval has been observed, additional risk factors must be considered. Patients who have sustained significant trauma or severe pain, particularly involving the head or chest, may experience delayed gastric emptying and a compromised gag reflex, further elevating aspiration risk [3]. Similarly, patients with medical conditions that predispose to aspiration regardless of fasting status, such as bowel obstruction or upper gastrointestinal bleeding, also require careful management [3]. Obstetric patients undergoing elective or emergent general anesthesia, especially beyond 18 weeks of gestation, represent another high-risk group, given physiological changes that affect gastric emptying and lower esophageal sphincter tone. Moreover, critically ill patients who require tracheal intubation due to altered mental status or other systemic compromise are inherently vulnerable to aspiration events. There are also patients for whom fasting status is simply unreliable. In such cases, regardless of the reported fasting duration, clinicians must adopt an approach that assumes the presence of a full stomach, particularly when the previously mentioned risk factors are present. When there is uncertainty, bedside gastric ultrasound can help confirm or rule out residual gastric contents.

Lastly, the growing use of GLP-1 receptor agonists raises new concerns about aspiration risk [5]. Emerging evidence, including gastric ultrasound and case reports, suggests that patients on GLP-1 may retain significant gastric contents despite standard fasting, increasing the risk of regurgitation during induction [6,7]. As use of these agents grows, awareness of their perioperative implications is essential for effective airway management and risk stratification. Notably, one large, retrospective study showed no increased risk of pulmonary aspiration with preoperative use of GLP-1 agents preoperatively, although medication withholding could not be verified [8].

Risks and complications of RSI

RSI is associated with substantial risk, with nearly 50% of patients experiencing at least one peri-intubation adverse event [9]. The most frequent complication is cardiovascular instability, reported in 42.6% of emergency intubations, but its definition varies depending on the study. For example, it is defined as systolic BP $<$ 65 mmHg, systolic BP $<$ 90 mmHg for $>$30 min, new or increased vasopressor requirement, or fluid bolus $>$15 mL/kg by Fjeld *et al.* or as mean BP $<$ 65 mmHg, or a drop of more than 30% in baseline mean BP between the start of anesthetic induction and the start of surgery by Sessler *et al.* [10,11]. Severe hypoxemia ($SpO_2 < 80\%$) and cardiac arrest were reported in 9.3% and 3.1% of cases, respectively. Failed or difficult intubation, particularly without ventilation between induction and intubation, increases the risk of hypoxia and hemodynamic collapse [12]. Achieving first-pass success (FPS) without complications is a key objective, as multiple laryngoscopy attempts are associated with increased adverse events in both hospital and prehospital settings [13–15]. While FPS failure is rare in surgical patients ($<$5%) due to VL use, it remains common in ICU and ED populations (up to 30%) [16,17]. Overall, RSI demands skilled execution, appropriate drug choices, and timely management of complications [18].

Techniques and evidence for reducing complications of RSI

1 **Preoxygenation:** Effective preoxygenation is critical to prevent peri-intubation hypoxemia during RSI in high-risk surgical or critically ill patients. Non-invasive ventilation (NIV) has consistently demonstrated superiority over standard face mask preoxygenation, including in hypoxemic patients, as shown in the PREOXI trial [19]. High-flow nasal oxygen (HFNO) offers apneic oxygenation and may be non-inferior in non-hypoxemic patients, but its efficacy is limited in severe hypoxemia [2,20]. The method (NIV + HFNO) has shown added benefit in preventing desaturation in hypoxemic patients [21]. A semi-upright position enhances preoxygenation, especially in obese patients. It is important to remember that gentle mask ventilation between induction and orotracheal intubation is feasible and reduces periprocedural hypoxemia without increasing the incidence of aspiration in the ICU [21]. In the operating room, this technique could be valuable for preventing desaturation during RSI in patients with an empty stomach; however, supporting evidence is currently limited. Lastly, in the absence of new, robust data favoring HFNO, NIV should remain the recommended approach for preoxygenation in patients requiring RSI [21].

2 ***Video Laryngoscope***: VL significantly improves first-pass success, particularly in high-risk patients undergoing endotracheal intubation across multiple hospital settings, including the operating room [18]. A recent NEJM study evaluating intubations in the ED and ICU also found that VL was associated with a higher first-pass success rate compared to direct laryngoscopy. Among surgical patients requiring single-lumen endotracheal intubation for general anesthesia, hyperangulated VL reduced the number of intubation attempts relative to direct laryngoscopy [18]. International guidelines now advocate for the routine and first-line use of VL in both emergency and elective airway management [22]. However, this practice is not yet widely adopted in the ED, where most clinicians still use direct laryngoscopy without a stylet [23].

3 **Stylet or Bougie**: The use of stylets and bougies has increased with the widespread adoption of videolaryngoscopy (VL), particularly given the variety of blade shapes available. Although VL improves glottic visualization, difficulties with advancing the endotracheal tube can persist. Some manufacturers now recommend routine stylet use even with Macintosh-style VL blades, in both normal and difficult airway scenarios [24]. However, stylet use carries risks, including rare but serious complications such as soft tissue perforation as well as more common minor adverse effects like postoperative pharyngeal pain and sore throat, reported in up to 50% of cases [25–28].

Importantly, a large multicenter randomized trial in critically ill patients demonstrated that stylet use significantly improves first-attempt intubation success compared to using the endotracheal tube alone [29]. Current high-quality evidence supports routine stylet use during VL, particularly in ICU and emergency settings. While cautious technique is needed to avoid complications, the benefits in terms of procedural success and patient safety are compelling. In surgical patients with optimized conditions, the benefit may be less dramatic but still present. Lastly, a multicenter randomized clinical trial involving 1,102 critically ill adults undergoing emergency intubation found no significant difference in first-pass success rates or incidence of severe desaturation between the use of a bougie and an endotracheal tube with a stylet [30].

4 **Cricoid Pressure:** Introduced by Sellick in 1961, cricoid pressure aimed to prevent aspiration by compressing the esophagus. Pressure is applied to the cricoid cartilage to compress the esophagus, aiming to reduce regurgitation [31]. The use of cricoid pressure to reduce aspiration risk in RSI is controversial due to insufficient evidence supporting its efficacy. MRI and clinical studies show that the esophagus may be laterally displaced and that cricoid pressure may impair laryngoscopy and ventilation [32]. In the IRIS Cricoid trial, there was no difference in aspiration between the cricoid and non-cricoid groups for RSI [33]. A higher rate of difficulty with intubation was noted in the cricoid group, but the result was not statistically significant. In a meta-analysis conducted in 2021 and including the IRIS trial, cricoid pressure did not have a negative impact on the successful first-attempt intubation rate or laryngoscopic view, but primarily in direct laryngoscopy (unlike videolaryngoscopy), and slightly prolongs intubation time and increases the risk of postoperative hoarseness [34]. Current consensus suggests applying cricoid pressure only if regurgitation occurs and promptly releasing it if it hinders intubation. Of note, cricoid pressure is contraindicated if there is concern for esophageal rupture and relatively contraindicated in cervical injury.

5 **Gastric Point of Care Ultrasound (POCUS):** Gastric ultrasound is a rapid and easy technique that can aid in the assessment of a patient's aspiration risk. The suggested view is a parasagittal view of the antrum while the patient is in a right lateral decubitus position, when patient movement is limited, such as in an emergency setting, rapid stomach evaluation can still be obtained in the supine position with or without head-of-bed elevation to 45 ° with 75–91% sensitivity for the diagnosis of gastric fluid volume $>$ 1.5 mL.kg^{-1} [35]. There is emerging evidence that gastric POCUS can serve as a useful predictor for aspiration risk in both the pre-operative setting as well as ED settings [36,37], and its teaching should be systematized, given the widespread availability of ultrasound in operating rooms in recent years.

6 **Nasogastric Tube (NGT) Management:** Nasogastric tube management during RSI remains controversial, and current evidence does not support routine NGT placement before induction solely to reduce aspiration risk. In patients who already have an NGT in place, suctioning and decompression may be beneficial in selected high-risk scenarios such as gastric outlet obstruction, ileus, massive gastric distension, or active upper gastrointestinal bleeding. Several societies, including the Society of Critical Care Medicine, recommend decompression in these specific contexts [38]. However, inserting an NGT immediately before RSI may provoke pain, gagging, or retching and paradoxically increase the risk of regurgitation. Moreover, routine placement has not been shown to reduce aspiration during induction [39].

Whether to remove an existing NGT before RSI should be individualized. An NGT may interfere with mask seal during preoxygenation or slightly hinder laryngoscopy, although the use of videolaryngoscopy reduces this impact. Conversely, leaving an NGT in place after suctioning may facilitate ongoing decompression in patients with known gastric distension and help prevent gastric insufflation during emergency positive-pressure ventilation. When feasible, bedside gastric ultrasound (GUS/POCUS) can assist in determining whether an NGT is necessary, guiding a tailored strategy for aspiration prevention in emergency and uncertain-fasting situations. Overall, NGT insertion or removal should be viewed as a selective intervention, reserved for cases with specific risk factors, rather than a routine component of RSI. Preoperative NGT management could be enhanced by the simultaneous use of GUS to help clinicians individualize aspiration-prevention strategies in the OR [40].

7 **Prophylactic Vasoactive Support:** Patients with impaired hemodynamic reserve may particularly benefit from targeted prophylactic vasopressor support. Individuals with a high shock index (HR/SBP $>$ 0.8), borderline MAP values ($<$75 mmHg), or low cardiac output states (e.g., severe heart failure, advanced valvular disease, sepsis-related myocardial depression) are disproportionately prone to cardiovascular collapse following induction [41]. In these populations, the abrupt reduction in systemic vascular resistance (SVR) or preload caused by propofol, etomidate, or even ketamine may precipitate profound hypotension, myocardial ischemia, or cardiac arrest. Early administration of phenylephrine (to support SVR) or low-dose norepinephrine infusion (0.02–0.06 μg/kg/min) immediately before or at the time of induction has been shown in observational analyses and pragmatic clinical practice to attenuate the drop in MAP and improve post-induction hemodynamic stability [42]. This approach is particularly relevant in patients with fixed outflow obstruction (e.g., severe aortic stenosis), pulmonary hypertension, or right ventricular dysfunction, where even modest reductions in MBP can compromise coronary and systemic perfusion [43,44]. While robust randomized data are still limited and formal guidelines have not endorsed universal prophylactic support, accumulating evidence suggests that a selective, physiology-based strategy is reasonable in patients with diminished cardiovascular reserve undergoing RSI.

8 **Prophylactic Fluid Administration:** Recent high-quality evidence does not support the routine use of a pre-induction fluid bolus to prevent peri-intubation hypotension. Both the PREPARE trial and the larger PREPARE II randomized clinical trial demonstrated that administering a crystalloid bolus prior to induction did not reduce the incidence of cardiovascular collapse, severe hypotension, or mortality among critically ill adults undergoing tracheal intubation [45]. These findings suggest that systematic fluid loading is largely ineffective in offsetting the hemodynamic instability associated with induction, especially when hypotension is driven primarily by vasodilation or impaired cardiac function rather than absolute hypovolemia [45]. As a result, pre-induction fluid boluses should not be recommended as a universal or protocolized strategy. Instead, fluid administration should be individualized and reserved for patients with clear clinical or ultrasound evidence of hypovolemia (e.g., prolonged fasting, gastrointestinal losses, severe third spacing, or recent hemorrhage), recognizing that excessive fluid administration carries its own risks in patients with cardiac dysfunction or ARDS.

Table 1 summarizes all these techniques, and Fig. 1 illustrates an updated timeline of RSI.

Lastly, a 2025 international survey by Ben-Naoui *et al.* confirmed substantial heterogeneity in RSI practices across 61 countries, particularly regarding opioid use, cricoid pressure,

Table 1
Author suggestions based on current literature.

Intervention	Evidence Summary	Suggestion Strength
Preoxygenation	Non-invasive ventilation (NIV) has consistently demonstrated superiority over standard face mask preoxygenation, including in hypoxemic patients. NIV should therefore be considered the first-line strategy for high-risk patients	Suggested
Video Laryngoscope	Strong evidence, particularly in difficult airways. Meta-analyses and RCTs support higher first-pass success and better glottic view *vs.* direct laryngoscopy, particularly in ICU and ED.	Suggested
Stylet or bougie	Stylet improves first-attempt intubation success compared to tracheal tube alone No difference between bougie and stylet	Suggested
Cricoid Pressure	Multiple RCTs and systematic reviews (e.g. IRIS trial) show no consistent benefit in preventing aspiration. May impair videolaryngoscopy and ventilation.	Not routinely suggested
Gastric POCUS	Available tool; moderate-quality evidence from observational studies and reviews. Can estimate gastric volume and detect solid/particulate content. Can be useful in patients under GLP-1 receptor agonists and SGLT-2 inhibitors	Conditionally suggested (as adjunct, particularly in uncertain aspiration risk)
Nasogastric Tube Placement	If already in place, consider suctioning to decompress the stomach Evidence suggests considering placement in individual high-risk cases if time permits, such as gastric outlet obstruction, bowel obstruction, or massive gastric distension Can interfere with adequate oxygenation and visualization	Conditionally suggested
Prophylactic Vasoactive Support	May reduce post-intubation hypotension Particular benefit for patients who are pre-load dependent or disproportionally sensitive to reduction in systemic vascular resistance (SVR), such as aortic stenosis No official recommendations	Suggested
Prophylactic Fluid Administration	Did not reduce the chance of hemodynamic instability Might cause more harm, particularly in critical care population	Not routinely suggested

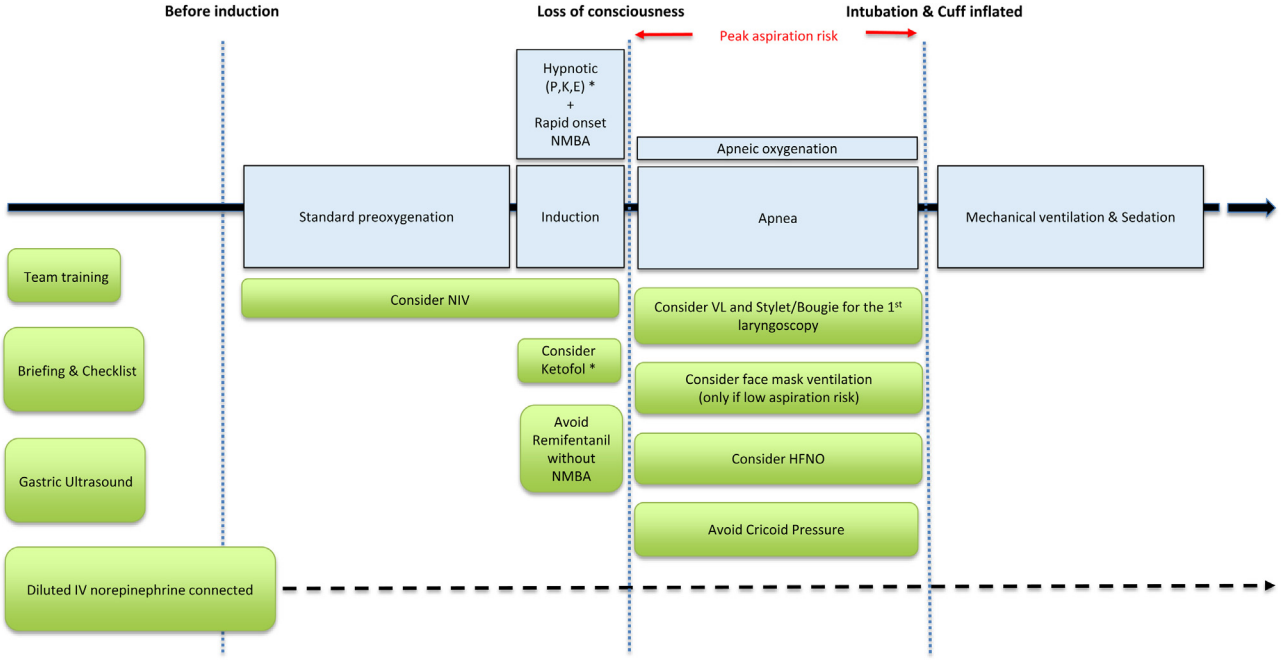

Fig. 1. Peri-Induction Timeline and Contemporary Modifications of Rapid Sequence Induction.

and indications for RSI in borderline cases such as GERD or obesity [46]. This underscores the pressing need for harmonized guidelines to minimize practice variation and improve patient safety. Complementing these findings, the 2023 Society of Critical Care Medicine published formal guidelines using GRADE methodology, recommending (albeit conditionally) semi-Fowler positioning, preoxygenation with high-flow nasal oxygen or NIV based on hypoxemia severity, and medication-assisted preoxygenation in uncooperative patients. These guidelines mark an important shift toward individualized, evidence-informed RSI strategies in critical care settings [38].

Pharmacologic agents for RSI

The selection of induction agents and neuromuscular blockers for RSI should be tailored to patient-specific characteristics, particularly in those who are critically ill or hemodynamically unstable.

Etomidate is a short-acting sedative used for RSI due to its rapid onset and hemodynamic stability. The recommended dose is 0.2–0.3 mg/kg administered as a single IV bolus. No dose adjustment is required based on toxicity during RSI, as it is administered as a one-time dose. Etomidate is a non-barbiturate sedative acting through GABA receptors, offering minimal cardiovascular effects, [47] making it an attractive choice for patients with hypotension or impaired cardiac reserve. While etomidate can cause adrenal suppression via inhibition of 11β-hydroxylase and increased susceptibility to infection in the ICU [48], the clinical significance of this effect following a single induction dose remains uncertain, particularly in the OR [49]. In a recent randomized trial published in the New England Journal of Medicine, ketamine was directly compared with etomidate for RSI in critically ill adults and was

associated with a higher incidence of peri-intubation cardiovascular collapse, especially among patients with sepsis and greater baseline severity of illness [50]. These findings suggest that etomidate may remain the preferred first-line induction agent for RSI in critically ill, septic, or hemodynamically unstable patients, in whom avoidance of cardiovascular collapse is a primary concern.

Propofol, a GABA potentiator, is widely used due to its rapid onset and short duration of action, as well as its antiemetic properties. However, its propensity for dose-dependent hypotension and myocardial depression may limit its use in unstable patients. The recommended dose is 2−3 mg/kg administered as a single IV bolus in hemodynamically stable patients. Propofol is now used for over 80% of patients in the OR, largely replacing others sedative [51,52].

Ketamine is a dissociative anesthetic with analgesic properties, widely used for RSI, particularly in hemodynamically unstable patients due to its ability to maintain blood pressure. The recommended dose is 1–2 mg/kg administered as a single IV bolus. No dose adjustment is required based on toxicity during RSI. There is increasing research to suggest that ketamine is associated with reduced mortality among critically ill patients who require tracheal intubation compared to etomidate [53]. It also preserves airway reflexes, which may be beneficial in selected scenarios. Combining ketamine and propofol (“ketofol”) allows clinicians to leverage the cardiovascular stability of ketamine with the sedative depth of propofol, achieving balanced anesthesia with reduced risk of hypotension [54,55]. While several case series suggest that ketofol may be a favorable induction agent in critically ill patients with cardiovascular compromise, further research is needed to better define its role and optimal use in this population.

The choice between etomidate and ketamine for RSI has long been debated, with prior observational data yielding conflicting results. Very recently, the multicenter RSI Trial randomized more than 2,000 critically ill adults undergoing emergency intubation in the emergency department or ICU. The trial, published in the *New England Journal of Medicine*, found no significant difference in 28-day all-cause in-hospital mortality between ketamine and etomidate (28.1% *vs.* 29.1%; adjusted absolute risk difference -0.8 percentage points [95% CI –4.5 to 2.9]; $P = 0.65$) [50]. However, ketamine was associated with a significantly higher incidence of cardiovascular collapse, the trial’s prespecified key secondary endpoint: 22.1% *vs.* 17.0% with etomidate (absolute risk difference 5.1 percentage points [95% CI 1.9–8.3]) [50].

Ciprofol and Remimazolam: Two newer hypnotic agents, ciprofol and remimazolam, have gained attention as potential alternatives for induction during RSI due to their favorable pharmacokinetic and hemodynamic profiles.

Ciprofol, a structural analog of propofol with higher potency at the GABA-A receptor, provides similar hypnotic depth at lower doses and has been associated with less injection pain and a lower incidence of hypotension in several early-phase trials [56]. It received regulatory approval for sedation of mechanically ventilated ICU patients in 2022, and small comparative studies suggest it may offer improved hemodynamic stability compared with propofol during induction [56]. Moreover, another small randomized control trial found benefit for hemodynamic stability for induction in patients with severe aortic stenosis compared to propofol [57]. However, evidence specific to RSI remains sparse, and isolated reports describe transient muscle fasciculations or mild elevations in liver enzymes. As of 2025, no major society has issued guidelines regarding its use for RSI, and additional trials are needed before widespread adoption.

Remimazolam, an ester-based benzodiazepine metabolized by tissue esterases, provides a rapid onset (typically 60–90 seconds), predictable offset, and a more favorable hemodynamic profile than propofol in both healthy and high-risk populations. Its reversible nature via flumazenil may appeal in certain RSI scenarios. Early studies and case reports describe effective intubating conditions when used with a neuromuscular blocker, and remimazolam may be particularly useful when avoidance of hypotension is critical. Nevertheless, robust data in emergency or critical care RSI remain limited, and optimal dosing strategies for rapid airway control are not yet established. Overall, both agents are promising but not yet validated for routine RSI, and their use should be individualized pending further evidence.

In contrast to commonly used induction agents, several drugs should be reconsidered during RSI due to the increased risk of peri-intubation complications. Although the Society of Critical Care Medicine includes midazolam as an acceptable option for RSI in select clinical circumstances, its pharmacologic profile is generally less favorable. Midazolam has a comparatively slower onset of action and can produce dose-dependent reductions in systemic vascular resistance and myocardial contractility, which can become more pronounced at the higher doses required for RSI. Accordingly, its use is best reserved for situations in which clear indications exist, such as active seizures [38,58]. A recent cohort study reported increased rates of peri-intubation hypotension and post-intubation ventilatory instability among critically ill adults receiving midazolam compared with ketamine or etomidate [59].

Concerning opioids, their use during RSI is a subject of debate [60]. Basically, opioids can be divided into two groups, depending on pharmacological duration: short with remifentanil or alfentanil and intermediate with sufentanil or fentanyl. For the latter, their administration immediately prior to induction is associated with abrupt decreases in systemic vascular resistance and bradycardia, contributing to severe post-induction hypotension [61]. A recent multicenter analysis demonstrated that pre-induction fentanyl was independently associated with higher rates of cardiovascular collapse during emergency airway management [62]. Their use might also interfere with the resumption of spontaneous breathing in cases of difficult intubation, but a strategy of this nature in a “full stomach” patient is questionable. Although they are also hypotensive, short-acting morphine derivatives have been proposed to limit the occurrence of tachycardia or hypertension induced by stimulation during laryngoscopy, which can cause harmful cardiac side effects in elderly or preeclamptic patients [63–65]. In any case, recent evaluation of RSI practice confirmed several changes with historical avoidance of opioids during RSI, with a systematic use in 69% of cases in a recent international survey [46].

Given these findings, routine use of midazolam or opioids during RSI in hemodynamically unstable patients should be avoided unless there is a compelling clinical indication, such as blunting the hypertensive response in severe arterial or intracranial hypertension. In ASA 1 or 2 patients, the safety of opioids during RSI before intubation should be investigated by further studies, particularly with a mind to minimizing the occurrence of post-induction hemodynamic complications.

Lidocaine has also been studied for use as an opioid-sparing method in RSI to decrease the likelihood of hemodynamic instability [66]. Growing evidence supports the use of intravenous lidocaine as an adjuvant during RSI, both as an opioid-sparing strategy and as a means of maintaining hemodynamic stability. Lidocaine blunts the sympathetic response to laryngoscopy, decreases anesthetic requirements, and may reduce the magnitude of blood pressure decline following induction [67]. In a randomized controlled trial, the administration of lidocaine 1 mg/kg before induction significantly reduced the required dose of propofol and was associated with greater hemodynamic stability compared with standard induction techniques [68]. Similarly, among older adults undergoing non-cardiac surgery, lidocaine combined with propofol resulted in lower rates of post-induction hypotension

compared with fentanyl–propofol combinations [69]. Although formal guidelines have not yet endorsed lidocaine as a routine component of RSI, the accumulating evidence supports considering lidocaine, particularly in hemodynamically unstable patients or when an opioid-sparing approach is desired.

Among neuromuscular blocking agents, succinylcholine, a depolarizing neuromuscular blocker, remains favored for its rapid onset (~30 seconds) and short duration of action (10–15 min). However, its use is contraindicated in several patient populations, including those with prolonged immobility or burn/crush injuries beyond 12–24 h due to the risk of severe hyperkalemia leading to fatal arrhythmias. The recommended dose is 1–1.5 mg/kg administered as a single IV bolus. No dose adjustment is required based on toxicity during RSI. Rocuronium, a non-depolarizing neuromuscular blocker, is the primary alternative when succinylcholine is contraindicated. Dosing is typically based on ideal body weight, although there is some debate regarding optimal dosing strategies for achieving a rapid onset in obese patients [70,71]. The recommended dose is 1–1.2 mg/kg administered as a single IV bolus. Rocuronium offers a longer duration of action (30–90 min), requiring attention to timely and adequate sedation depth to prevent awareness post-intubation [1]. This drug's effects can be rapidly and predictably reversed with sugammadex, enabling return to a train?of?four ratio $\geq$0.9 within minutes and significantly shorter extubation times compared to neostigmine. The expiration of its original patent (RE'733) in many countries in 2024 has opened the market to generic versions, leading to a substantial reduction in the cost of sugammadex [72].

Finally, remifentanil has been studied as an alternative to neuromuscular blockers in patients at risk of aspiration. In a recent randomized trial, remifentanil did not meet non-inferiority criteria for first-pass intubation success compared to neuromuscular blockers, although the clinical relevance of this difference remains uncertain [73]. Thus, neuromuscular blockers remain the standard approach for facilitating optimal intubating conditions during RSI, and remifentanil is an alternative solution when neuromuscular blockers need to be avoided [74].

Sequence order: Although sedative-first administration is standard during RSI, some centers, particularly in EDs and ICUs, have explored giving the neuromuscular blocker first to shorten the time to intubation [75]. Available data suggest no increased risk of awareness with this approach, but supporting evidence derives largely from prehospital settings with limited monitoring, and its clinical benefit remains uncertain [75–77]. In routine in-hospital RSI, administering the hypnotic agent before the paralytic remains the standard practice.

Preparation for RSI

Careful preparation of the patient is a critical step in optimizing outcomes during RSI. Proper positioning plays a key role: placing the patient in a head-elevated or reverse Trendelenburg position can enhance preoxygenation and prolong safe apnea time, particularly in obese or critically ill patients. Effective preoxygenation is essential to maximize oxygen reserves and delay desaturation during apnea; this is typically achieved with 100% oxygen via a tight-fitting face mask or preferably with NIV, with a recommended duration of at least three minutes or eight vital-capacity breaths. Establishing reliable vascular access is equally important, as RSI relies on prompt administration of induction and neuromuscular blocking agents and rapid treatment of potential hemodynamic instability. Whenever feasible, large-bore intravenous access should be secured prior to induction, and a second line may be advisable in high-risk cases. Meticulous attention to these preparatory steps enhances both the safety and efficiency of RSI and helps mitigate the risk of complications in vulnerable patients. In the ICU, this safety-oriented approach using an intubation management protocol led to a significant reduction of the incidence of life-threatening complications occurring within 60 min after intubation (cardiac arrest or death, severe cardiovascular collapse, and hypoxemia) [78].

Conclusion

Fifty-five years after its introduction, RSI continues to evolve. In 2025, RSI must strike a careful balance between preventing aspiration and minimizing hypoxemia and hemodynamic instability. While foundational components such as preoxygenation and rapid drug administration remain essential, a more flexible and nuanced approach has emerged. Routine cricoid pressure is no longer recommended; gentle ventilation and apneic oxygenation are safe in appropriately selected patients. When available, VL with a stylet should be the first-line approach to maximize first-pass success, which remains a critical goal alongside the prevention of desaturation and post-induction hypotension. Ketamine and etomidate are favored induction agents for hemodynamically unstable patients. Importantly, success in RSI depends not only on pharmacology and technique, but also on human factors, effective teamwork, and the use of cognitive aids.

Future research should focus on optimizing preoxygenation strategies, clarifying the role and timing of gastric ultrasound, defining the place of opioids in RSI, and evaluating pharmacologic combinations such as ketofol, which may help reduce post-induction hypotension. In addition, structured, team-based approaches aligned with universal airway management principles, as recently proposed by the Project for Universal Management of Airways, offer an opportunity to standardize practice, reduce cognitive load, and enhance interdisciplinary collaboration [79]. Such strategies hold promise for improving overall RSI performance and patient outcomes.

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